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| APPLICATION NO.   | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO.        | CONFIRMATION NO.       |
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| 10/578,965  | 05/10/2006  | Markus Luy           | 2024.5                     | 8557                   |
| 7590  | 02/26/2010  |                      |                            |                        |
| Scott E Hanf<br>Hammer & Hanf<br>Suite G<br>3125 Springbank Lane<br>Charlotte, NC 28226 |             |                      | EXAMINER<br>AFREMOVA, VERA |                        |
|   |             |                      | ART UNIT<br>1657           | PAPER NUMBER           |
|   |             |                      | MAIL DATE<br>02/26/2010    | DELIVERY MODE<br>PAPER |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

|                              |                                      |                                   |
|------------------------------|--------------------------------------|-----------------------------------|
| <b>Office Action Summary</b> | <b>Application No.</b><br>10/578,965 | <b>Applicant(s)</b><br>LUY ET AL. |
|                              | <b>Examiner</b><br>Vera Afremova     | <b>Art Unit</b><br>1657           |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If no period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 29 October 2009.

2a) This action is FINAL.      2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1,2,4-6 and 8-20 is/are pending in the application.

4a) Of the above claim(s) 14-20 is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1,2,4-6, 8-13 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All    b) Some \* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO/GS-68)  
 Paper No(s)/Mail Date \_\_\_\_\_

4) Interview Summary (PTO-413)  
 Paper No(s)/Mail Date \_\_\_\_\_

5) Notice of Informal Patent Application

6) Other: \_\_\_\_\_

**DETAILED ACTION**

Claims 1, 2, 4-6, 8-13 as amended (10/29/2009) are under examination in the instant office action.

This application contains claims 14-20 drawn to invention(s) nonelected with traverse in the reply filed on 5/06/2008. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

***Claim Rejections - 35 USC § 112***

Claims 1, 2, 4-6, 8-13 as amended are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 as amended now recites “adjusting” pH value with “a corresponding acid or a base” that does not correspond to CaCO<sub>3</sub> because it is either generic or it is NaOH in the light of specification (page 8, lines 26-28; page 10, line 18; page 12, line 19). However, the invention is directed to the use of CaCO<sub>3</sub> as essential means for pH value stabilization as claimed, as disclosed and as argued. Thus, the claim as amended is contradictory and, therefore, indefinite. Further, the phrase “adjusting the pH value of said fermentation” also appears to encompass some active manipulation of pH during fermentation to the value 5-7 that is set prior to fermentation. The claim as amended is confusing and, therefore, indefinite. It is suggested to write, for example: “wherein in the pH value of the fermentation medium is set prior to the start of the fermentation in the range of ... “as it is disclosed in the specification.

The same rejection is applied to claim 13 as amended. With respect to claim 13 it is noted that the end of the last phrase missing or cut out as result of typing error.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 2, 4-6, 8-13 as amended are/remain rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,582,941 (Yokochi et al), US 6,509,178 (Tanaka et al), EP 0 113 183 (IDS reference) and Bajpai et al. (IDS reference).

Claims are directed to a method for cultivating microorganisms belonging to *Thraustochytriales* wherein the method comprise step of cultivating the microorganisms belonging to *Thraustochytriales* in a fermentation medium comprising calcium carbonate in amounts 3-15 g/L as means for pH stabilization and step of isolating PUFAs, wherein the starting pH value is about 5-7; and, wherein the microorganisms bring forth production of more than 10% DHA per unit of weight of dry biomass. Some claims are further drawn to production of oils and DPA. Some claims are further drawn to cultivation conditions such as temperature between 10 and 40 degree C and cultivation time 1-10 days. Some claims are further drawn to the use of fermentation medium comprising glucose, corn steep liquor, potassium hydrogen phosphate, ammonium sulfate, magnesium and calcium chloride, calcium carbonate and sodium sulfate. Some claims are further drawn to culturing microorganisms belonging to *Thraustochytriales* such as *Schizachytrium sp.* strain SR21 and *Ulkenia sp.* strain SAM 2179.

US 6,582,941 (Yokochi et al) and US 6,509,178 (Tanaka et al) teach methods for cultivation of microorganisms belonging to *Thraustochytriales* as intended for production of

DHA and DPA. The cited methods include cultivation of the *Thraustochytriales* representatives such as *Schizachytrium* sp. strain SR21 (US 6,582,941 at abstract and table 7) and *Ulkenia* sp. strain SAM 2179 (US 6,509,178 at abstract and table 1). The disclosed cultivation conditions are within the presently claimed ranges of cultivation conditions that they include pH 4-6.5 temperature between 10 and 35 degree C and cultivation time 3-7 days. The disclosed fermentation media contain same nutrients as required by the claimed invention including glucose, corn steep liquor, potassium hydrogen phosphate, ammonium sulfate and sea salts that comprise magnesium and calcium chloride, calcium carbonate and sodium sulfate at least to some extent. For example: see US 6,582,941 at col. 10, lines 66-67; col.11, lines 1-3; col.18, lines 14-20. For example: see US 6,509,178 at col. 7, lines 50-57; col. 8, lines 1-14.

The method of the cited patents result in accumulation or production of more than 10% DHA per biomass weigh and more than 1 % of DPA per biomass weigh. For example: US 6,582,941 discloses accumulation or production by SR21 strain of more 10% DHA per weigh (see table 7; 7.2 g/L of DHA and 39.6g/L biomass; 54% total fat per weight and 34 % DHA per total fat). The cited US 6,509,178 also discloses accumulation or production by SAM 2179 strain of more than 10% DHA per weigh and more than 1 % DPA (table 1).

The cited patents US 6,582,941 (Yokochi et al) and US 6,509,178 (Tanaka et al) teach pH control during cultivation of microorganisms belonging to *Thraustochytriales* but the cited references only disclose the use of a generic suitable acid and/or base material, thus, being silent about calcium carbonate as material for pH adjustments.

However, EP 0 113 183 teaches the pH control during microbial cultivation with pH controlling material such as calcium carbonate (see abstract) including concentrations 0.5-5 g/L

in fermentation medium (page 9, lines 9-11). Further, the reference by Bajpai et al. teaches cultivation of microbial representatives of *Thraustochytriales* in a fermentation medium with calcium carbonate (at “materials and methods” and Fig. 1).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to use calcium carbonate as pH controlling material during cultivation of microorganisms belonging to *Thraustochytriales* with a reasonable expectation of success in culturing the microorganisms belonging to *Thraustochytriales* because the prior art prior art teaches the use of calcium carbonate as pH controlling material as adequately taught by EP 0 113 183 and because microorganisms belonging to *Thraustochytriales* have been cultured in the presence of calcium carbonate as intended for oils, DHA and DPA production as evidenced by Bajpai et al. The claimed specific strains SR 21 and SAM 2179 have been known and cultured in the fermentation methods as intended for oils, DHA and DPA production as adequately demonstrated by US 6,582,941 (Yokochi et al) and US 6,509,178 (Tanaka et al).

Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references.

Therefore, the claims are properly rejected under 35 USC § 103.

#### ***Response to Arguments***

Applicant's arguments filed 10/29/2009 have been fully considered but they are not persuasive.

With regard to claim rejection under 35 USC § 103 applicants argue that the cited references US 6,582,941 (Yokochi et al) and US 6,509,178 (Tanaka et al) teach the use of starting pH values much lower than the presently claimed pH 5-7 (response page 9, par. 1). Upon review of the references it is not found particularly true because pH ranges in the methods of the cited patents are overlapping with the presently claimed ranges. For example: US 6,582,941 (Yokochi et al) teaches the pH range 4-6.5 (col.10, line 67); US 6,509,178 (Tanaka et al) teaches the pH range 3-8 (col.4, line 51).

Further, with regard to the teaching of the cited EP 0 113 183 (Carson) about calcium carbonate as pH controlling material applicants appear argue that the teaching of this reference is not analogous art because the disclosed method is used for alcoholic fermentation by yeasts (response pages 12-13). This argument is not found particularly convincing because the cited EP 0 113 183 (Carson) clearly teaches that calcium carbonate is used for neutralizing acidic materials that are released or produced during fermentation of sugar-containing solutions (page 3, lines 1-10; page 5, lines 10-20). One of skill in the art would clearly recognize that culturing any and all groups of microbes would benefit from the use of optimal pH and the cited EP 0 113 183 explicitly teaches the use of calcium carbonate as pH controlling agent in microbial fermentations and, in particular, for neutralizing acidic materials.

Further, with regard to Bajpai et al. Applicants argue (response page 12) that the cited document discloses the use of calcium carbonate for culturing *Thraustochytriales* at concentration lower than it is required by the instant claims and that the cited document demonstrates lower production of microbial biomass, oils and DHA than achieved by Applicants. This argument does not have any persuasive grounds because Bajpai et al. clearly demonstrate

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that the representatives of *Thraustochytriales* have been cultured in the prior art in the presence of calcium carbonate as intended for oils, DHA and DPA production and because the claimed invention is solely directed to culturing *Thraustochytriales* and it does not require recovery of products as argued and/or intended.

As a whole with regard to claim rejection under 35 USC § 103 applicants argue that there is no suggestion or motivation to combine or modify the teaching of the cited references (response pages 7-11, for example). However, the cited references are in the same field of endeavor (such as culturing microorganism at optimal pH and conditions) and they seek to solve the same problems as the instant application and claims (such as optimization of microbial culturing processes as intended for manufacturing of edible products), and one of skill in the art is free to select and/or to modify components available in the prior art, *In re Winslow*, 151 USPQ 48 (CCPA, 1966).

Although examiner recognizes that references cannot be arbitrarily combined that there must be some reason why one skilled in the art would be motivated to make the proposed combination of primary and secondary references, *In re Nomiya*, 184 USPQ 607 (CCPA 1975). However, there is no requirement that a motivation to make the modification be expressly articulated. One test for combining references is what the combination of disclosures taken as a whole would suggest to one versed in the art, rather than by their specific disclosures, *In re Bozek*, 163 USPQ 545 (CCPA 1969). In this case, the use of calcium carbonate as a pH control agent during cultivation/fermentation of microorganisms is known in the prior art as evidenced by the teaching of EP 0 113 183 and the microorganisms belonging to *Thraustochytriales* have

been successfully cultured in the presence of calcium carbonate as intended for oils, DHA and DPA production as evidenced by Bajpai et al.

Applicants' arguments as based on unexpected effects such as increase in biomass, oil and DHA production by *Thraustochytriales* microorganisms (response page 9, par. 2) have been fully considered but not found persuasive for the very least reasons the evidence necessary to overcome a *prima facie* case of obviousness must not only be clear and convincing, but must also be commensurate in scope with the claimed subject matter. The scope of the showing must be commensurate with the scope of claims to consider evidence probative of unexpected results, for example. In re Dill, 202 USPQ 805 (CCPA, 1979), In re Lindner 173 USPQ 356 (CCPA 1972), In re Hyson, 172 USPQ 399 (CCPA 1972), In re Boesch, 205 USPQ 215, (CCPA 1980), In re Grasselli, 218 USPQ 769 (Fed. Cir. 1983), In re Clemens, 206 USPQ 289 (CCPA 1980).

In the instant case, the unexpected results as argued are based on biomass, oil and DHA production by 2 strains that are *Ulkenia sp.* SAM 2179 (specification table 1) and *Schizochytrium sp.* SR 21 (specification table 5). Yet, the pending claims 1, 2 4-6, 8-10 and 13 are broadly directed culturing the generic representatives of the order of *Thraustochytriales*.

Further, with respect to the particular claims 11 and 12 that encompass the use of particular strains *Ulkenia sp.* SAM 2179 and *Schizochytrium sp.* SR 21 it is noted that these strains are known in the prior art and they were used in the fermentation methods for production of oils, DHA and DPA as adequately demonstrated by US 6,582,941 (Yokochi et al) and US 6,509,178 (Tanaka et al). Moreover, the cited documents demonstrate biomass, oils and/or DHA production by these particular strains as presently recited in the pending claims 1, 2 and 4. For example: US 6,582,941 discloses accumulation or production by SR21 strain of more than 10%

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DHA per weight or about 10 % (biomass 39.6 g/L and 7.2 g/L DHA; see table), about 54% of oil or total fat per weight (table 7). The cited US 6,509,178 (Tanaka et al) discloses production of more than 1 % DPA or 1.3 % DPA (see table 1) by the strain SAM 2179 strain and more than 10% DHA or about 25% DHA (biomass 19.5 g/l and DHA 5.5 g/L; see table 1).

Thus, the scope of pending claims do not commensurate with the scope of showing as argued.

No claims are allowed.

***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber, can be reached at (571) 272-0925.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

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February 25, 2010

/Vera Afremova/  
Primary Examiner, Art Unit 1657